Department of Pesticide Regulation

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Process for Human Health Risk Assessment Prioritization and Initiation

Risk assessment plays a critical role in the California Department of Pesticide Regulation's (DPR) evaluation of the potential hazards to human health associated with pesticide exposure. Risk assessment is a process designed to answer questions about how toxic a chemical is, what exposure results from its various uses, what is the likelihood that use will cause harm, and how to characterize that risk. DPR takes a comprehensive approach to risk assessment and assesses potential dietary, workplace, residential, and ambient air exposures. Risk assessment is often the driving force behind new regulations and other use restrictions.

Assessing pesticide risks is a dynamic process, evolving with advancements in science and with changes in pesticide use patterns. Initiating a risk assessment on a specific pesticide is based on choosing the pesticide that poses the greatest potential risk. Risk assessments may be initiated for a number of reasons. For example, the identification of possible adverse health effects during review of toxicology data submitted under the Birth Defect Prevention Act may trigger a risk assessment. Similarly, a risk assessment may be initiated when use of a pesticide may result in exposures of concern from ambient air, or from programs to eradicate exotic pest infestations.

Regardless of the impetus for initiating the risk assessment, DPR sets priorities for risk assessments through a single process. Setting priorities is critical to making the best use of staffing and other resources, and to ensure that the Department focuses on chemicals with the greatest potential risk.

DPR has modified its priority-setting process to make it more consistent, understandable, and transparent. This document describes the prior process, the elements that DPR has added, and the way in which priority-setting will be documented.

Setting priorities for initiating risk assessments is focused on ensuring that the pesticides that pose the greatest risk are evaluated and ensuring that the prioritization process does not delay the initiation of risk assessments.

Outline of Candidate Selection Process

1) High, Medium, Low Grouping
   An interdepartmental Adverse Effects Advisory Panel places active ingredients into one of three groups: high, medium or low priority for risk assessment.

2) Annual Candidate Pool
   Each year DPR senior scientists identify and prioritize a smaller group of 10 candidates for risk assessment initiation.

3) Selection Process
   - 3.1) Recommended candidates – Based on staffing and other resources, DPR determines how many risk assessments can be initiated in the coming year.
   - 3.2) Prioritizing the candidate pool -- Senior DPR scientists and branch chiefs make recommendations to upper management on the specific active ingredients that should enter the risk assessment process.
   - 3.3) Public consultation - The recommendations are made available to interested parties, posted on DPR's Web site, and presented to the interagency Pesticide Registration and Evaluation Committee (PREC) and the Scientific Review Panel (SRP) for review and comment. DPR will also include corresponding descriptive documents for the 10 active ingredients in the candidate pool.

4) Initiation of Risk Assessment
   - 4.1) After evaluating comments, the Department decides which pesticide active ingredients should enter the risk assessment process.
   - 4.2) Risk assessments are initiated through a formal notification process.

Grouping of Active Ingredients

The High, Medium, Low Grouping process has been in effect for a number of years and will remain unchanged. The remaining steps are either new or have been modified to ensure that decisionmaking is well-documented and understandable to interested parties.

Active ingredients now entering the prioritization process generally have the complete toxicology database required for federal registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). While this FIFRA data serves as the primary source of toxicity information, scientific staff will consider other reliable data during both the prioritization and risk assessment processes. Because a comprehensive exposure database is generally not available at the time of prioritization, estimates of exposure potential are based on the best available information. The prioritization process itself may also serve to identify the need for additional toxicity and exposure data.

The initial grouping for risk assessment involves evaluation by the Adverse Effects Advisory Panel. This panel is made up of senior scientists from three DPR branches—Medical Toxicology, Worker Health and Safety, and Environmental Monitoring—and from Cal/EPA's Office of Environmental Health Hazard Assessment (OEHHA). The panel uses the criteria described below to group active ingredients into high, moderate, or low categories for risk assessment.

This process is qualitative, using a weight-of-evidence approach to identify active ingredients most likely to present significant health risks. No greater weight is given to any single criteria or

group of criteria. After the panel reaches a consensus on groupings, its conclusions are presented in a formal report at a public meeting of DPR's Pesticide Registration and Evaluation Committee (PREC).

The Adverse Effects Advisory Panel meets periodically to update the groupings as new active ingredients are added or deleted, or new data becomes available that can affect priorities. (Active ingredients are deleted when risk assessments are completed or registrations are cancelled.)

Determining the Pool of Candidates for Risk Assessment

In a new procedure, senior scientists from DPR's Worker Health and Safety, Environmental Monitoring and the Medical Toxicology branches will further refine priorities. DPR will invite a senior scientist from OEHHA and from the Air Resources Board (ARB) to participate in this step of the process. Drawing on their expertise in and detailed knowledge of pesticides, these scientists will select 10 active ingredients (drawn primarily from the panel's high-priority category) for further examination.

The scientists will review the physical-chemical properties, toxicity, and exposure potential of the 10 compounds to determine the level of concern for each chemical in each criteria grouping. A summary document will be prepared for each of the 10 active ingredients that describes how each chemical meets the listed criteria. On the basis of this evaluation, the candidates will be ranked in priority from 1 to 10.

When a risk assessment is initiated, the chemical will be removed from the candidate pool. DPR senior scientists (along with the invited OEHHA and ARB senior scientists) will review the candidate list annually, in part to add new chemicals to replace those deleted. At the same time, they will review new information (such as additional toxicology or exposure data, or recent regulatory actions by DPR or other state or federal agencies) and as a result, may modify the rankings or remove pesticides from the candidate list.

Selecting Active Ingredients for Risk Assessment Initiation

Annually, DPR analyzes staffing and other resources to determine how many risk assessments can be initiated in the coming year. Then, working from the candidate pool rankings, senior scientists and branch chiefs from the Medical Toxicology, Worker Health and Safety, and Environmental Monitoring branches recommend specific active ingredients on which to begin risk assessments. These recommendations will be forwarded, through programmatic Assistant Directors, to the DPR Chief Deputy Director.

Once the recommendations are approved, the Department will announce active ingredients it proposes to enter the risk assessment process and begin a 45-day comment period. The announcement will be posted on DPR's Website and sent to interested parties including the

Scientific Review Panel. The announcement will also include corresponding descriptive documents for the 10 active ingredients in the candidate pool, along with their ranking. This information will also be presented at a meeting of the PREC for the members' advice and comments. After evaluating comments, the Department will decide which pesticide active ingredients will enter the risk assessment process. The Department will continue to publish a formal "Notice to Registrants" with this information.

Criteria Used to Set Priorities

The criteria used to prioritize all active ingredients for risk assessment and to identify those that could pose the greatest health risks can be divided into three categories: physical and chemical properties, toxicity, and exposure. Other considerations that may also impact prioritization include eradication programs for new pests, and regulatory actions by other state or federal agencies.

The ***physical-chemical properties*** of an active ingredient may affect the manner and degree to which it will be released into and persist in the environment, available for human exposure. A higher vapor pressure, for example, may increase the inhalation risk for both occupational and ambient air exposures. A longer half-life under various environmental conditions may enhance the persistence of the material, thus increasing the potential for greater and repeated human exposure. A chemical that is more soluble in water may be more likely to move into drinking water by leaching through the soil into groundwater, or via runoff into surface water. On the other hand, greater soil binding—while decreasing the potential for movement into sources of drinking water—could increase environmental persistence and the potential for exposure if soil particles become airborne and are inhaled. While not necessarily a physical-chemical property, the propensity of a chemical to bioaccumulate or bioconcentrate is also an important consideration.

If all other factors are equal, greater ***toxicity*** of a material results in greater risk. The prioritization process considers a number of factors that may raise or lower the toxicological concern. For example, two compounds may cause different effects at the same dose level. The magnitude or severity of these effects may differ significantly. The compounds may differ in the number of reported effects or the number of species responding in toxicology studies. They may also differ in the seriousness of the response. For example, eye irritation will not generally present the same level of concern as convulsions or cancer. The scientists will also consider whether the effects are systemic (e.g., neurotoxicity) or local (e.g., skin irritation).

Two compounds may cause the same effect, but one compound may cause the effects at a significantly lower dosage. In determining priorities, scientists compare severity of effects among compounds and the timeframe before onset. Another consideration is the shape of the dose-response curve, that is, the relationship between dose and response. A steep curve (where a small change in dose can greatly increase toxicity) may have significantly different consequences

than one where large changes in dose are required for an effect. The mechanism of action, if known, will also be considered. In some cases, the mechanism of action may impact the level of concern for an effect seen in animal studies in terms of being relevant to people. Toxic effects seen in humans, such as those identified through epidemiological studies or illness reports, may be considered in conjunction with animal data to determine the level of toxicological concern.

As with toxicity, if all other factors are equal, greater ***exposure*** results in greater risk. During the prioritization process, potential exposure is characterized based on available information. The types of potential exposures are important considerations (for example, occupational, residential, ambient air, food residue, drinking water). Use patterns (for example, agriculture, residential, or manufacturing) and projected changes in use can have a major impact on the human exposures. If a pesticide is applied infrequently and only on a single ornamental crop, it will generally be prioritized lower than one with uses on a large number of crops. Prioritization also takes into account anticipated changes in use patterns, such as when a pesticide is intended as a replacement for another widely used pesticide.

Typical locations where a pesticide may be used will also be considered. For example, if a pesticide is often used in or near residential communities, the higher population density means that more people could be affected by exposure via ambient air or offsite movement than if the pesticide is only used in rural areas with lower population density.

Methods of application also have a potentially significant impact on exposure. Air-blast or aerial applications may generate aerosols that can increase inhalation as well as dermal exposures. These modes of application also increase the possibility of offsite and ambient exposures due to air exposures. Application rate obviously has a direct impact, since application rates can range from ounces (or fractions of an ounce) per acre to pounds per acre (or hundreds of pounds in the case of fumigants).

The type of formulation may have a large impact on exposure, with less potential exposure using granular formulations, enclosed baits, or tree trunk injections than for wettable powders mixed in solution or dust formulations applied directly to a crop site.

Illness surveillance data are also valuable indicators of exposure potential, demonstrating that the potential is real, not theoretical. All other elements being equal, the availability of monitoring and other exposure data may give one compound priority over another, since this allows the risk assessment to proceed without waiting for such data to be generated.

Initiating the Risk Assessment

DPR intends that risk assessments be comprehensive and consider all appropriate exposure routes and scenarios (e.g., oral, inhalation, dermal, occupational, residential, industrial, institutional, bystander, dietary, ambient air, water). When active ingredients enter risk

assessment, DPR toxicologists determine if additional data are needed and, if so, request it from the appropriate sources. Data may be requested or required from the registrants (possibly through DPR's formal reevaluation process). DPR may also conduct surface and ground water monitoring and/or exposure monitoring to generate data. If adequate ambient air data are not available, the ARB may also be requested to conduct air monitoring.

The risk assessment is prepared in the form of a risk characterization document (RCD). The RCD assembles, critiques, and interprets all pertinent scientific data on a chemical's toxicology, human experience, and exposure.

Selection of Active Ingredients That May Go Through the TAC Process

The prioritization and risk assessment process will take into account our mandate to evaluate the ambient air risks from pesticides. Pesticides that meet established criteria will be designated as toxic air contaminants (TAC) after a specific review and evaluation process. To complement our comprehensive risk assessment process and the toxic air contaminant mandate, we will evaluate every pesticide through the risk assessment process as a possible TAC candidate. Generally, fumigant pesticides will automatically be TAC candidates as they go through the risk assessment process.

For other pesticides, we will make specific evaluations as the risk assessment proceeds through the hazard identification stage, and screening reference doses (RfDs) and screening air reference concentrations (RfCs) are calculated. If adequate ambient air data are available, the screening RfCs are compared with the monitored air levels. Projected changes in use patterns are also evaluated for their potential impact on ambient air.

(The RfD is an estimate of the daily exposure of the human population to a chemical, usually by the oral route, that is likely to be without adverse effects. The RfC is an estimate of the daily air concentration of a chemical that is likely to be without adverse effects to the exposed human population. RfCs and RfDs may be developed for acute, subchronic, and chronic exposure periods. Screening values, although not regulatory standards, can be used to evaluate monitoring results.)

If monitored and projected ambient air levels are well below those concentrations that would meet the regulatory criteria for identification as a TAC (CCR Title 3, Division 6, Section 6890), it would be unlikely that the chemical would be listed as a TAC. In these instances, DPR would not submit the chemical to the TAC Scientific Review Panel (SRP) for consideration. However, the draft RCD would be sent to ARB and OEHHA for comments on the ambient air section.

If monitored or projected ambient air concentrations are near or above those concentrations that would meet the criteria for identification as a TAC (CCR Title 3, Division 6, Section 6890), DPR

will initiate the TAC process. The RCD will be prepared with an extensive section on ambient air and will be submitted to the SRP for review and evaluation.

If the RCD is ready for completion without adequate ambient air data, the RCD will be finalized with a section on ambient air describing the current status and anticipated concerns. An addendum covering ambient air may be generated later and a decision could be made to pursue TAC listing should the data support this action.

In certain instances, ambient air monitoring data may not be necessary to recognize that an active ingredient (a fumigant, for example) has the potential to be a TAC. In these cases, it could be inappropriate to delay the TAC process and it would be initiated concurrently with the risk assessment. Ambient air monitoring may still be requested from the ARB and/or required from the registrants, to be used in the control phase (to determine appropriate control measures).